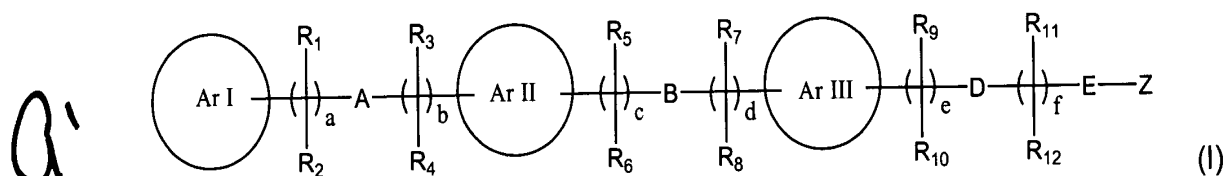


1. (Twice Amended) A compound of formula I

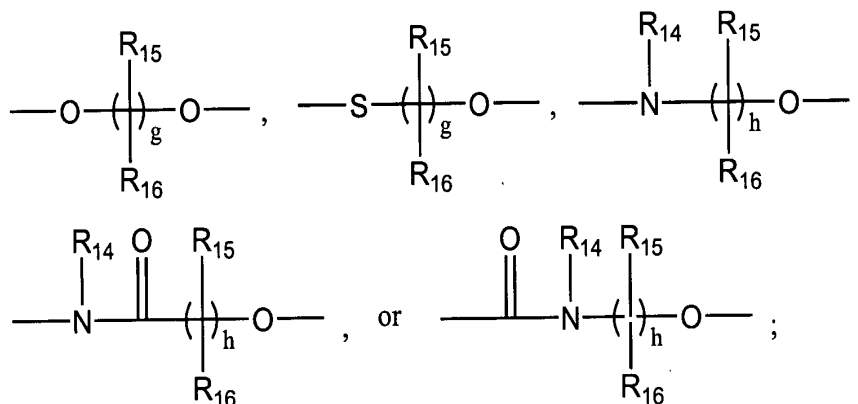


wherein:

Ar I is heteroaryl, which is optionally substituted by one or more ring system substituents;

Ar II and Ar III are, independently, aryl, which are optionally substituted by one or more ring system substituents;

A is -O-, -S-, -SO-, -SO₂-, -NR₁₃-, -C(O)-, -N(R₁₄)C(O)-, -C(O)N(R₁₅)-,
-N(R₁₄)C(O)N(R₁₅)-, -C(R₁₄)=N-, a chemical bond,



B is -O-, -S-, -SO-, -SO₂-, -NR₁₇-, ethynylene, -C(O)-, -N(R₁₈)C(O)-, or -C(O)NR₁₈-;

D is -O-, -S-, -NR₁₉-, a chemical bond, ethynylene, -N(R₂₀)C(O)-, -C(O)-, or
-C(O)N(R₂₀)-;

E is a chemical bond or an ethylene group;

a is 0-4;

b is 0-4;

a'

c is 0-4;

d is 0-5;

e is 0-4;

f is 0-6;

g is 1-4;

h is 1-4;

R₁, R₃, R₅, R₇, R₉, and R₁₁, are independently hydrogen, halogen, alkyl, carboxyl, alkoxycarbonyl or aralkyl;

R₂, R₄, R₆, R₈, R₁₀ and R₁₂, are independently $-(CH_2)_q-X$;

q is 0-3;

X is hydrogen, halogen, alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroaralkyl, hydroxy, alkoxy, aralkoxy, heteroaralkoxy, carboxyl, alkoxycarbonyl,

tetrazolyl, acyl, acylHNSO₂⁻, -SR₂₃, Y¹Y²N- or Y³Y⁴NCO-;

Y¹ and Y² are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl, or one of Y¹

and Y² is hydrogen or alkyl and the other of Y¹ and Y² is acyl or aroyl;

Y³ and Y⁴ are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl;

Z is R₂₁O₂C-, R₂₁OC-, cyclo-imide, -CN, R₂₁O₂SHNCO-, R₂₁O₂SHN-, (R₂₁)₂NCO-, R₂₁O-2,4-thiazolidinedionyl, or tetrazolyl; and

R₂₁ is hydrogen, alkyl, aryl, cycloalkyl, or aralkyl;

R₁₃, R₁₇, R₁₉ and R₂₃ are independently R₂₂OC-, R₂₂NHOC-, hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, heteroaralkyl, or aralkyl;

R₁₄, R₁₅, R₁₆, R₁₈ and R₂₀ are independently hydrogen, alkyl, aralkyl, carbonyl, or alkoxycarbonyl;

or R₁₄, and R₁₅ taken together with the carbon and nitrogen atoms through which they are linked form a 5 or 6-membered azaheterocyclyl group; or

when a is 2-4, then vicinal R₁ radicals taken together with the carbon atoms to which the R₁ radicals are linked form an ethylene group; or

when b is 2-4, then vicinal R₃ radicals taken together with the carbon atoms to which the R₃ radicals are linked form an ethylene group; or

when c is 2-4, then vicinal R₅ radicals taken together with the carbon atoms to which the R₅ radicals are linked form an ethylene group; or

when d is 2-5, then vicinal R₇ radicals taken together with the carbon atoms to which the R₇ radicals are linked form an ethylene group; or

a' when e is 2-4, then vicinal R₉ radicals taken together with the carbon atoms to which the R₉ radicals are linked form an ethylene group; or

when f is 2-6, then vicinal R₁₁ radicals taken together with the carbon atoms to which the R₁₁ radicals are linked form an ethylene group; and

R₂₂ is hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, heteroaralkyl, or aralkyl; or

a pharmaceutically acceptable salt thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof;

wherein

"alkyl" is an aliphatic hydrocarbon group which is straight or branched having 1 to about 20 carbon atoms and is optionally substituted by one or more alkyl group substituents;

"aryl" is an aromatic monocyclic or multicyclic ring system of about 6 to about 14 carbon atoms, which is optionally substituted by one or more ring system substituents;

"heteroaryl" is an aromatic monocyclic or multicyclic ring system of about 5 to about 14 carbon atoms, in which at least one of the carbon atoms in the ring system is replaced by nitrogen, oxygen or sulfur, which is optionally substituted by one or more ring system substituents;

"heterocyclyl" is a non-aromatic saturated monocyclic or multicyclic ring system of 3 to about 10 carbon atoms, in which at least one of the carbon atoms in the ring system is replaced by nitrogen, oxygen or sulfur, which is optionally substituted by one or more ring system substituents;

"heteroaralkyl" is a heteroaryl-alkyl group, wherein the heteroaryl and alkyl groups are as defined above;

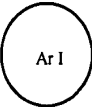
an "alkyl group substituent" is halo, carboxy, cycloalkyl, cycloalkenyl, heterocyclyl, heterocyclenyl, aryl, alkoxy, alkoxycarbonyl, aralkoxycarbonyl,

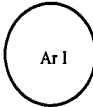
heteroaralkoxycarbonyl, or Y^1Y^2NCO- , wherein Y^1 and Y^2 are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl, or Y^1 and Y^2 taken together with the nitrogen atom to which Y^1 and Y^2 are attached form heterocyclyl

wherein the substituents may contain further alkyl group substituents or ring system substituents as recited herein; and

a "ring system substituent" is alkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroaralkyl, hydroxy, alkoxy, aryloxy, aralkoxy, acyl, aroyl, halo, nitro, cyano, carboxy, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, alkylsulfonyl, arylsulfonyl, heteroarylsulfonyl, alkylsulfinyl, arylsulfinyl, heteroarylsulfinyl, alkylthio, arylthio, heteroarylthio, aralkylthio, heteroaralkylthio, fused cycloalkyl, fused cycloalkenyl, fused heterocyclyl, fused heterocyclenyl, arylazo, heteroarylazo, R^aR^bN- , R^cR^dNCO- , R^cO_2CN- , or $R^cR^dNSO_2-$ wherein R^a and R^b are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl, or one of R^a and R^b is hydrogen or alkyl and the other of R^a and R^b is aroyl or heteroaroyl, and R^c and R^d are independently hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, cycloalkenyl, heterocyclyl, heterocyclenyl, aralkyl or heteroaralkyl and, where the ring is cycloalkyl, cycloalkenyl, heterocyclyl or heterocyclenyl, the ring system substituent may also include methylene, oxo and thioxo on carbon atoms thereof,

wherein the substituents may contain further alkyl group substituents or ring system substituents as recited herein.

2. (Amended) A compound according to claim 1 wherein  is optionally substituted azaheteroaryl.

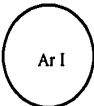
20. (Twice Amended) A compound according to claim 1 wherein  is an optionally substituted quinolinyl, quinoxalinyl, quinazolinyl, isoquinolinyl, benzoxazolyl, benzimidazolyl, benzothiazolyl, benzofuranyl, benzothiophenyl, oxazolyl, thiazolyl,

oxadiazolyl, isoxazolyl, imidazolyl, pyrazol-yl, thiadiazolyl, triazolyl, pyridyl, pyrimidinyl, pyrazinyl, or pyridazinyl group.

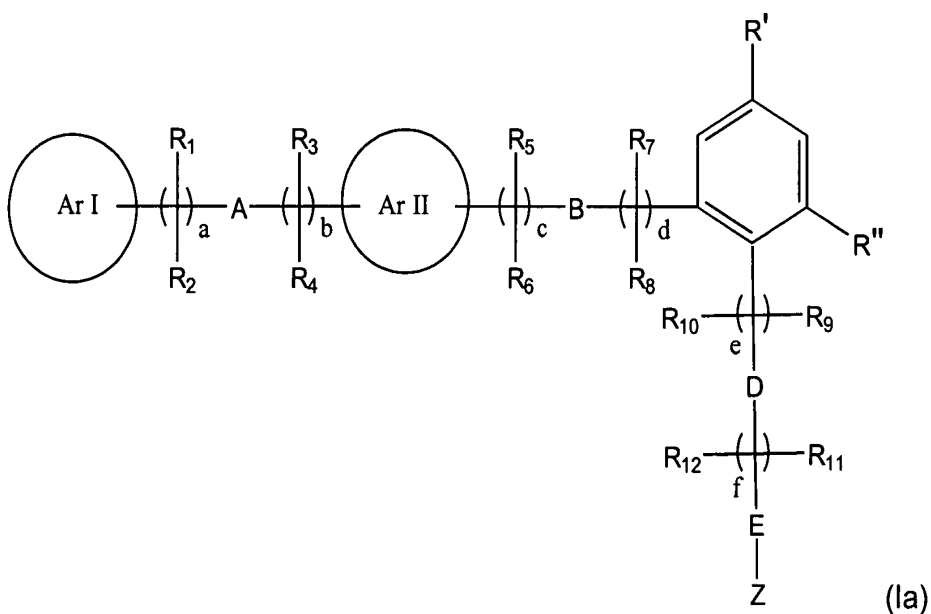
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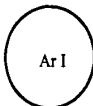
21. (Amended) A compound according to claim 1 wherein is unsubstituted quinolin-2-yl, 3-substituted quinolin-2-yl, 4-substituted quinolin-2-yl, 6-substituted quinolin-2-yl or 7 substituted quinolin-2-yl; an unsubstituted quinoxalin-2-yl, 3-substituted quinoxalin-2-yl, 6-substituted quinoxalin-2-yl or 3,6-disubstituted quinoxalin-2-yl; unsubstituted quinazolin-2-yl, 4-substituted quinazolin-2-yl or 6-substituted quinazolin-2-yl; unsubstituted isoquinolin-3-yl, 6-substituted isoquinolin-3-yl or 7-substituted isoquinolin-3-yl; 2-substituted-oxazol-4-yl or 2,5 disubstituted-oxazol-4-yl; 4-substituted oxazol-2-yl or 4,5-disubstituted-oxazol-2-yl; 2-substituted thiazol-4-yl or 2,5-disubstituted thiazol-4-yl; 4-substituted thiazol-2-yl or 4,5-disubstituted-thiazol-2-yl; 5-substituted-[1,2,4]oxadiazol-3-yl; 3-substituted-[1,2,4] oxadiazol-5-yl; 5-substituted-imidazol-2-yl or 3,5-disubstituted-imidazol-2-yl; 2-substituted-imidazol-5-yl or 2,3-disubstituted-imidazol-5-yl; 3-substituted-isoxazol-5-yl; 5-substituted-isoxazol-3-yl; 5-substituted-[1,2,4] thiadiazol-3-yl; 3-substituted-[1,2,4]-thiadiazol-5-yl; 2-substituted-[1,3,4]-thiadiazol-5-yl; 2-substituted-[1,3,4]-oxadiazol-5-yl; 1-substituted-pyrazol-3-yl; 3-substituted-pyrazol-5-yl; 3-substituted-[1,2,4]-triazol-5-yl; 1-substituted-[1,2,4]-triazol-3-yl; 3-substituted pyridin-2-yl, 5-substituted pyridin-2-yl, 6-substituted pyridin-2-yl or 3,5-disubstituted pyridin-2-yl; 3-substituted pyrazin-2-yl, 5-substituted pyrazin-2-yl, 6-substituted pyrazin-2-yl or 3,5 disubstituted-pyrazin-2-yl; 5-substituted pyrimidin-2-yl or 6-substituted-pyrimidin-2-yl; 6-substituted-pyridazin-3-yl or 4,6-disubstituted-pyridazin-3-yl; unsubstituted -benzothiazol-2-yl or 5-substituted-benzothiazol-2-yl; unsubstituted benzoxazol-2yl or 5-substituted-benzoxazol-2yl; unsubstituted -benzimidazol-2-yl or 5-substituted-benzimidazol-2-yl; unsubstituted -thiophen-2yl, 3-substituted -thiophen-2yl, 6-substituted -thiophen-2yl or 3,6-disubstituted-thiophen-2yl; unsubstituted -benzofuran-2-y, 3-substituted-benzofuran-2-yl, 6-substituted-benzofuran-2-yl or 3,6-disubstituted-benzofuran-2-yl; 3-substituted-benzofuran-6-yl or 3,7-disubstituted-benzofuran-6-yl.

Q² 22. (Amended) A compound according to claim 21 wherein  is substituted by a substituent selected from the group consisting of phenyl, substituted-phenyl, thienyl, substituted thienyl, cycloalkyl, straight or branched lower alkyl, fluoro, chloro, alkoxy, aralkyloxy, trifluoromethyl and trifluoromethyloxy.

Q³ 27. (Twice Amended) A compound of formula (Ia)

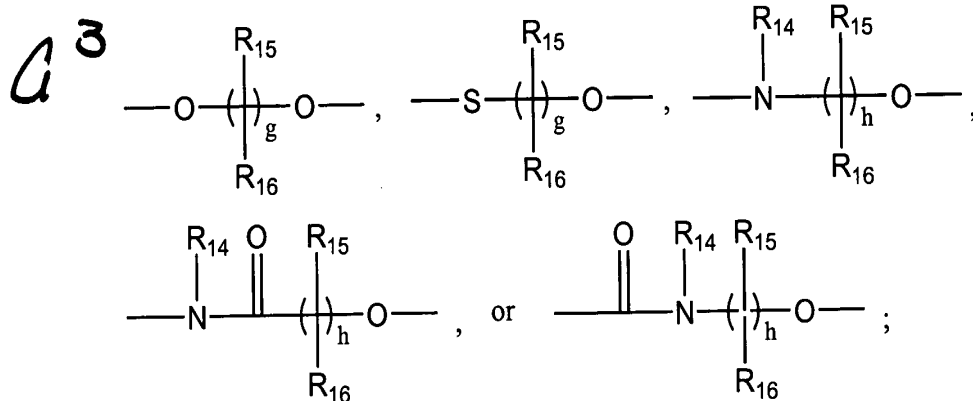


wherein:

 is heteroaryl, which is optionally substituted by one or more ring system substituents;

 is aryl, which is optionally substituted by one or more ring system substituents;

A is -O-, -S-, -SO-, -SO₂-, -NR₁₃-, -C(O)-, -N(R₁₄)C(O)-, -C(O)N(R₁₅)-,
-N(R₁₄)C(O)N(R₁₅)-, -C(R₁₄)=N-, a chemical bond,



B is -O-, -S-, -SO-, -SO₂-, -NR₁₇-, ethynylene, -C(O)-, -N(R₁₈)C(O)-, or -C(O)NR₁₈-;

D is -O-, -S-, -NR₁₉-, a chemical bond, ethynylene, -N(R₂₀)C(O)-, -C(O)-, or
-C(O)N(R₂₀)-;

E is a chemical bond or an ethylene group;

a is 0-4;

b is 0-4;

c is 0-4;

d is 0-5;

e is 0-4;

f is 0-6;

g is 1-4;

h is 1-4;

R₁, R₃, R₅, R₇, R₉, and R₁₁, are independently hydrogen, halogen, alkyl, carboxyl,
alkoxycarbonyl or aralkyl;

R₂, R₄, R₆, R₈, R₁₀ and R₁₂, are independently -(CH₂)_q-X;

q is 0-3;

X is hydrogen, halogen, alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl,
heteroaralkyl, hydroxy, alkoxy, aralkoxy, heteroaralkoxy, carboxyl, alkoxycarbonyl,
tetrazolyl, acyl, acylHNSO₂-, -SR₂₃, Y¹Y²N- or Y³Y⁴NCO-;

Y^1 and Y^2 are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl, or one of Y^1 and Y^2 is hydrogen or alkyl and the other of Y^1 and Y^2 is acyl or aroyl;

Y^3 and Y^4 are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl;

Z is $R_{21}O_2C-$, $R_{21}OC-$, cyclo-imide, $-CN$, $R_{21}O_2SHNCO-$, $R_{21}O_2SHN-$, $(R_{21})_2NCO-$, $R_{21}O-$ 2,4-thiazolidinedionyl, or tetrazolyl;

R' and R'' are, independently, hydrogen or ring system substituents;

R_{21} is hydrogen, alkyl, aryl, cycloalkyl, or aralkyl;

R_{13} , R_{17} , R_{19} and R_{23} are independently $R_{22}OC-$, $R_{22}NHOC-$, hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, heteroaralkyl, or aralkyl;

R_{14} , R_{15} , R_{16} , R_{18} and R_{20} are independently hydrogen, alkyl, aralkyl, carbonyl, or alkoxycarbonyl;

or R_{14} , and R_{15} taken together with the carbon and nitrogen atoms through which they are linked form a 5 or 6-membered azaheterocyclyl group; or

when a is 2-4, then vicinal R_1 radicals taken together with the carbon atoms to which the R_1 radicals are linked form an ethylene group; or

when b is 2-4, then vicinal R_3 radicals taken together with the carbon atoms to which the R_3 radicals are linked form an ethylene group; or

when c is 2-4, then vicinal R_5 radicals taken together with the carbon atoms to which the R_5 radicals are linked form an ethylene group; or

when d is 2-5, then vicinal R_7 radicals taken together with the carbon atoms to which the R_7 radicals are linked form an ethylene group; or

when e is 2-4, then vicinal R_9 radicals taken together with the carbon atoms to which the R_9 radicals are linked form an ethylene group; or

when f is 2-6, then vicinal R_{11} radicals taken together with the carbon atoms to which the R_{11} radicals are linked form an ethylene group; and

R_{22} is hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, heteroaralkyl, or aralkyl;

or

a pharmaceutically acceptable salt thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

36. (Amended) A compound according to claim 27 wherein:

a = 1;

A is -O-;

b = 0;

c = 0;

B is -O-;

d = 1;

e = 0;

f = 0;

D and E are a chemical bond;

R' is hydrogen;

R" is methyl;

Z is -CO₂H.

51. (Amended) A method according to claim 50 wherein the physiological disorder is associated with a physiological detrimental blood level of insulin, glucose, free fatty acids (FFA), or triglycerides.

58. (Amended) The method according to claim 51, wherein the physiological disorder is a cardiovascular condition.

68. (Amended) A method according to claim 67 wherein the physiological disorder is associated with a physiological detrimental blood level of insulin, glucose, free fatty acids (FFA), or triglycerides.

75. (Amended) The method according to claim 67, wherein the physiological disorder is a cardiovascular disorder.

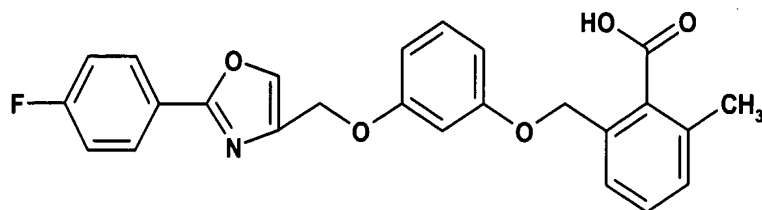
89. (Amended) A compound as claimed in claim 20, wherein the ring system substituent is selected from the group consisting of phenyl, substituted-phenyl, thienyl, substituted thienyl, cycloalkyl, straight or branched lower alkyl, fluoro, chloro, alkoxy, aralkyloxy, trifluoromethyl and trifluoromethoxy.

a¹⁰

91. (Amended) A compound as claimed in claim 31, wherein Rⁿ is methyl.

94. (Amended) A compound as claimed in claim 1, wherein the compound is

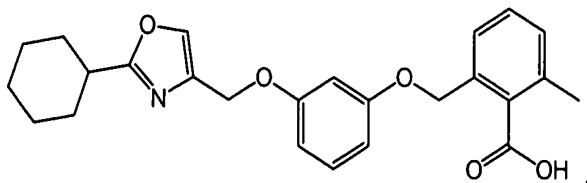
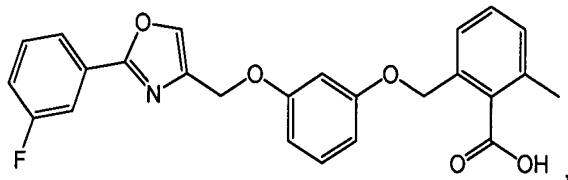
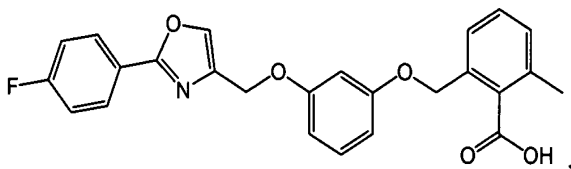
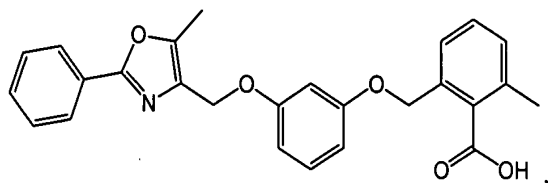
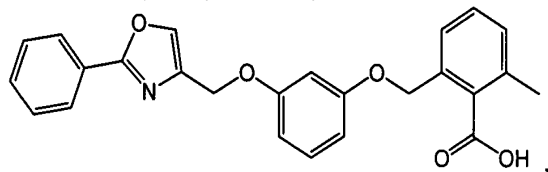
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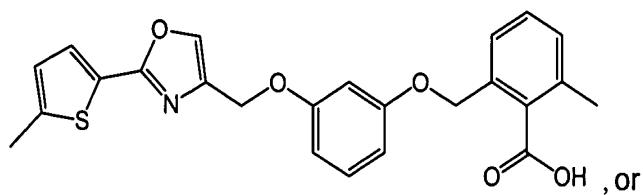


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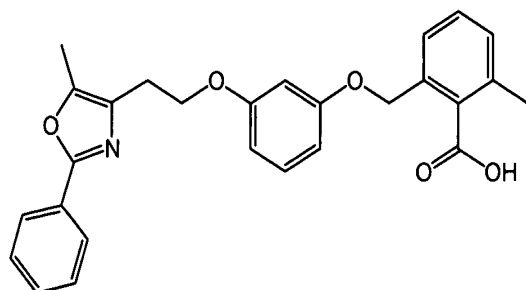
or a pharmaceutically acceptable salt, hydrate or solvate thereof.

95. (New) A compound as claimed in claim 1, wherein the compound is



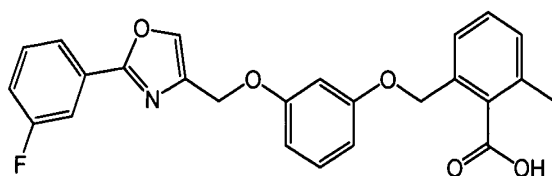
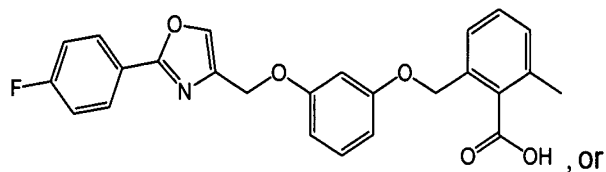
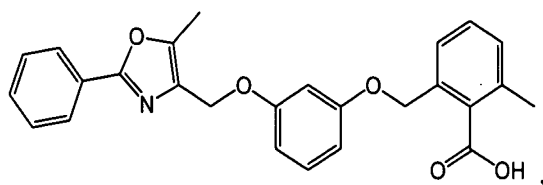
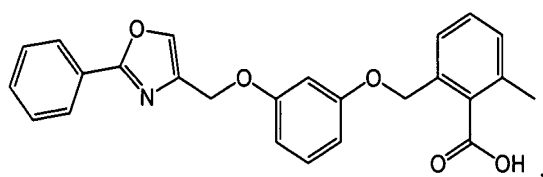


a¹¹



or a pharmaceutically acceptable salt, hydrate or solvate thereof.

96. (New) A compound as claimed in claim 1, wherein the compound is



or a pharmaceutically acceptable salt, hydrate or solvate thereof.